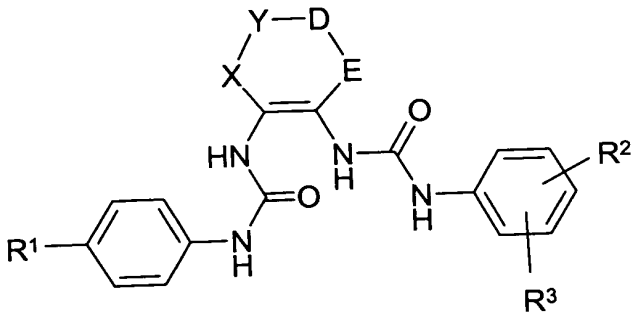
Patent Claims

1. Compounds of the formula I



I

in which

X-Y-D-E denotes CH=CH-CH=CH, N=CH-CH=CH, CH=N-CH=CH, CH=CH-N=CH, CH=CH-CH=N, N=CH-N=CH, CH=N-CH=N, $N^+(-O^-)$=CH-CH=CH, CH=$N^+(-O^-)$-CH=CH, CH=CH-$N^+(-O^-)$=CH, CH=CH-CH=$N^+(-O^-)$, NH-CO-CH=CH, CH=CH-CO-NH, CO-NH-CH=CH, CH=CH-NH-CO, in which the H atoms of the -CH- groups may be substituted by Hal, A, OH, OA, A-COO-, Ph-$(CH_2)_n$-COO-, cycloalkyl-$(CH_2)_n$-COO-, A-CONH-, A-CONA-, Ph-CONA-, N_3, NH_2, NO_2, CN, COOH, COOA, $CONH_2$, CONHA, $CON(A)_2$, O-allyl, O-propargyl and/or O-benzyl,

Ph denotes phenyl which is unsubstituted or mono-, di- or trisubstituted by A, OA, OH or Hal,

R^1 denotes Hal, -C≡C-H, -C≡C-A, OH or OA,

R^2 denotes H, Hal or A,

R^3 denotes 2-oxo-1*H*-pyridin-1-yl, 2-oxo-1*H*-pyrazin-1-yl, 2-oxopiperidin-1-yl, 2-oxopyrrolidin-1-yl, 2-oxo-1,3-oxazinan-3-yl, 3-oxomorpholin-4-yl, 2-oxotetrahydro-

pyrimidin-1-yl, 3-oxo-2*H*-pyridazin-2-yl, 4-oxo-1*H*-pyridin-1-yl, 2-oxoimidazolidin-1-yl, 2,6-dioxopiperidin1-yl, 2-oxopiperazin-1-yl, 2,6-dioxopiperazin-1-yl, 2,5-dioxopyrrolidin-1-yl, 2-oxo-1,3-oxazolidin-3-yl, 2-caprolactam-1-yl (= 2-oxoazepan-1-yl), 2-azabicyclo[2.2.2]-octan-3-on-2-yl, 5,6-dihydro-1*H*-pyrimidin-2-oxo-1-yl, 4*H*-1,4-oxazin-4-yl, 2-iminopiperidin-1-yl, 2-iminopyrrolidin-1-yl, 3-iminomorpholin-4-yl, 2-iminoimidazolidin-1-yl or 2-imino-1*H*-pyrazin-1-yl, each of which is unsubstituted or mono- or disubstituted by A, OH and/or OA,

A denotes unbranched, branched or cyclic alkyl having 1-10 C atoms, in which, in addition, 1-7 H atoms may be replaced by F and/or chlorine,

Hal denotes F, Cl, Br or I,

n denotes 0, 1, 2 or 3,

and pharmaceutically usable derivatives, solvates, salts and stereoisomers thereof, including mixtures thereof in all ratios.

2. Compounds according to Claim 1 in which

R^1 denotes Hal or -C≡C-H,

and pharmaceutically usable derivatives, solvates, salts and stereoisomers thereof, including mixtures thereof in all ratios.

3. Compounds according to Claim 1 or 2 in which

R^1 denotes Hal,

and pharmaceutically usable derivatives, solvates, salts and stereoisomers thereof, including mixtures thereof in all ratios.

4. Compounds according to one or more of Claims 1-3 in which

X-Y-D-E denotes CH=CH-CH=CH, N=CH-CH=CH, CH=N-CH=CH, CH=CH-N=CH, CH=CH-CH=N,

N=CH-N=CH, CH=N-CH=N, $N^+(-O^-)$=CH-CH=CH, CH=$N^+(-O^-)$-CH=CH, CH=CH-$N^+(-O^-)$=CH, CH=CH-CH=$N^+(-O^-)$, NH-CO-CH=CH, CH=CH-CO-NH, CO-NH-CH=CH or CH=CH-NH-CO,

in which the H atoms of the -CH- groups may be substituted by Hal, A, OH and/or OA,

and pharmaceutically usable derivatives, solvates, salts and stereoisomers thereof, including mixtures thereof in all ratios.

5. Compounds according to one or more of Claims 1-4 in which

X-Y-D-E denote CH=CH-CH=CH, N=CH-CH=CH, CH=N-CH=CH, CH=CH-N=CH, CH=CH-CH=N, N=CH-N=CH, CH=N-CH=N, $N^+(-O^-)$=CH-CH=CH, CH=$N^+(-O^-)$-CH=CH, CH=CH-$N^+(-O^-)$=CH or CH=CH-CH=$N^+(-O^-)$,

in which the H atoms of the -CH- groups may be substituted by Hal, OH and/or OA,

and pharmaceutically usable derivatives, solvates, salts and stereoisomers thereof, including mixtures thereof in all ratios.

6. Compounds according to one or more of Claims 1-5 in which

R^3 denotes 2-oxo-1*H*-pyridin-1-yl, 2-oxo-1*H*-pyrazin-1-yl, 2-oxopiperidin-1-yl, 2-oxopyrrolidin-1-yl, 2-oxo-1,3-oxazinan-3-yl, 3-oxomorpholin-4-yl, 2-oxotetrahydropyrimidin-1-yl, 3-oxo-2*H*-pyridazin-2-yl, 4-oxo-1*H*-pyridin-1-yl, 2-oxoimidazolidin-1-yl or 2-oxopiperazin-1-yl,

and pharmaceutically usable derivatives, solvates, salts and stereoisomers thereof, including mixtures thereof in all ratios.

7. Compounds according to one or more of Claims 1-6 in which

R^3 denotes 2-oxo-1*H*-pyridin-1-yl or 3-oxomorpholin-4-yl,

and pharmaceutically usable derivatives, solvates, salts and stereoisomers thereof, including mixtures thereof in all ratios.

8. Compounds according to one or more of Claims 1-7 in which

X-Y-D-E denotes CH=CH-CH=CH, N=CH-CH=CH, CH=N-CH=CH, CH=CH-N=CH, CH=CH-CH=N, N=CH-N=CH, CH=N-CH=N, $N^+(-O^-)$=CH-CH=CH, CH=$N^+(-O^-)$-CH=CH, CH=CH-$N^+(-O^-)$=CH or CH=CH-CH=$N^+(-O^-)$,
in which the H atoms of the -CH- groups may be substituted by Hal, OH and/or OA,

R^1 denotes Hal,

R^2 denotes H, Hal or A,

R^3 denotes 2-oxo-1*H*-pyridin-1-yl, 2-oxo-1*H*-pyrazin-1-yl, 2-oxopiperidin-1-yl, 2-oxopyrrolidin-1-yl, 2-oxo-1,3-oxazinan-3-yl, 3-oxomorpholin-4-yl, 2-oxotetrahydropyrimidin-1-yl, 3-oxo-2*H*-pyridazin-2-yl, 4-oxo-1*H*-pyridin-1-yl, 2-oxoimidazolidin-1-yl or 2-oxopiperazin-1-yl,

A denotes unbranched, branched or cyclic alkyl having 1-10 C atoms, in which, in addition, 1-7 H atoms may be replaced by F and/or chlorine,

Hal denotes F, Cl, Br or I,

and pharmaceutically usable derivatives, solvates, salts and stereoisomers thereof, including mixtures thereof in all ratios.

9. Compounds according to Claim 1 selected from the group

1-(4-chlorophenyl)-3-(4-hydroxy-2-{3-[3-methyl-4-(3-oxomorpholin-4-yl)phenyl]ureido}phenyl)urea,

1-(4-chlorophenyl)-3-(4-{3-[3-methyl-4-(3-oxomorpholin-4-yl)-phenyl]ureido}pyridin-3-yl)urea,

1-(4-chlorophenyl)-3-(4-{3-[3-methyl-4-(3-oxomorpholin-4-yl)-phenyl]ureido}-1-oxypyridin-3-yl)urea,

1-(2-chloro-4-{3-[3-methyl-4-(3-oxomorpholin-4-yl)phenyl]-ureido}pyridin-3-yl)-3-(4-chlorophenyl)urea,

1-(2-chloro-4-{3-[3-chloro-4-(3-oxomorpholin-4-yl)phenyl]-ureido}pyridin-3-yl)-3-(4-chlorophenyl)urea,

1-(4-chlorophenyl)-3-(4-hydroxy-2-{3-[4-(2-oxo-2*H*-pyridin-1-yl)phenyl]ureido}phenyl)urea,

1-(4-chlorophenyl)-3-(3-{3-[3-methyl-4-(3-oxomorpholin-4-yl)-phenyl]ureido}pyridin-2-yl)urea,

1-(4-chlorophenyl)-3-(3-{3-[3-methyl-4-(3-oxomorpholin-4-yl)-phenyl]ureido}-1-oxypyridin-4-yl)urea,

1-(4-chlorophenyl)-3-(5-hydroxy-2-{3-[3-methyl-4-(3-oxomorpholin-4-yl)phenyl]ureido}phenyl)urea,

1-(4-chlorophenyl)-3-(4-hydroxy-2-{3-[2-fluoro-4-(3-oxomorpholin-4-yl)phenyl]ureido}phenyl)urea,

1-(4-chlorophenyl)-3-(4-hydroxy-2-{3-[2-methyl-4-(3-oxomorpholin-4-yl)phenyl]ureido}phenyl)urea,

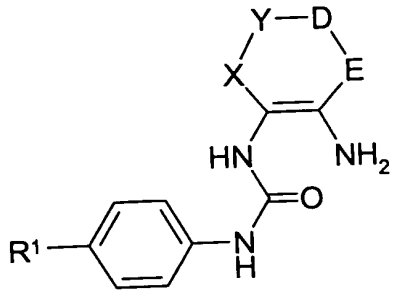
1-(4-chlorophenyl)-3-(3-{3-[2-fluoro-4-(3-oxomorpholin-4-yl)-phenyl]ureido}-1-oxypyridin-4-yl)urea,

1-(4-chlorophenyl)-3-(3-{3-[2-methyl-4-(3-oxomorpholin-4-yl)-phenyl]ureido}-1-oxypyridin-4-yl)urea,

and pharmaceutically usable derivatives, solvates, salts and stereoisomers thereof, including mixtures thereof in all ratios.

10. Process for the preparation of compounds of the formula I according to Claims 1-9 and pharmaceutically usable derivatives, solvates, salts and stereoisomers thereof, characterised in that

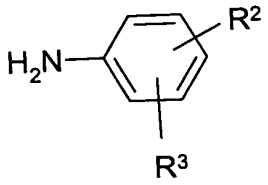
a) a compound of the formula II



II

in which X-Y-D-E and R^1 have the meanings indicated in Claim 1, is reacted with a chloroformate derivative to give an intermediate carbamate derivative,

which is subsequently reacted with a compound of the formula III

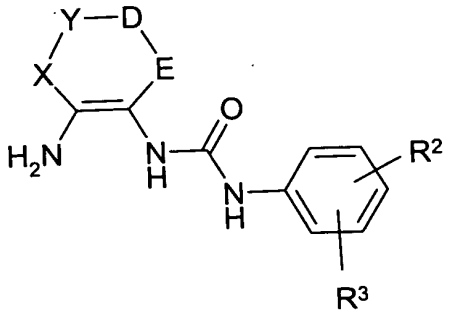


III

in which
R^2 and R^3 have the meanings indicated in Claim 1,

or

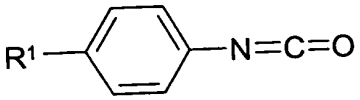
b) a compound of the formula IV



IV

in which X-Y-D-E, R^2 and R^3 have the meanings indicated in Claim 1,

is reacted with a compound of the formula V



V

in which R^1 has the meaning indicated in Claim 1,

or

c) a radical X-Y-D-E is converted into another radical X-Y-D-E by oxidising the radical X-Y-D-E,
and/or a base or acid of the formula I is converted into one of its salts.

11. Compounds of the formula I according to one or more of Claims 1 to 9 as inhibitors of coagulation factor Xa.

12. Compounds of the formula I according to one or more of Claims 1 to 9 as inhibitors of coagulation factor VIIa.

13. Medicaments comprising at least one compound of the formula I according to one or more of Claims 1 to 9 and/or pharmaceutically usable derivatives, solvates and stereoisomers thereof, including mixtures thereof in all ratios, and optionally excipients and/or adjuvants.

14. Medicaments comprising at least one compound of the formula I according to one or more of Claims 1 to 9 and/or pharmaceutically

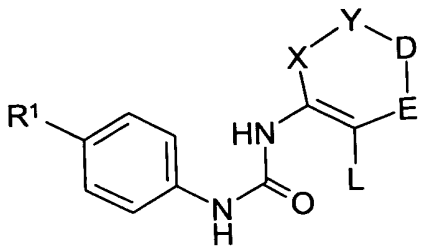
usable derivatives, solvates and stereoisomers thereof, including mixtures thereof in all ratios, and at least one further medicament active ingredient.

15. Use of compounds according to one or more of Claims 1 to 9 and/or physiologically acceptable salts and solvates thereof for the preparation of a medicament for the treatment of thromboses, myocardial infarction, arteriosclerosis, inflammation, apoplexy, angina pectoris, restenosis after angioplasty, claudicatio intermittens, migraine, tumours, tumour diseases and/or tumour metastases.

16. Set (kit) consisting of separate packs of
(a) an effective amount of a compound of the formula I according to one or more of Claims 1 to 9 and/or pharmaceutically usable derivatives, solvates and stereoisomers thereof, including mixtures thereof in all ratios,
and
(b) an effective amount of a further medicament active ingredient.

17. Use of compounds of the formula I according to one or more of Claims 1 to 9 and/or pharmaceutically usable derivatives, solvates and stereoisomers thereof, including mixtures thereof in all ratios, for the preparation of a medicament for the treatment of thromboses, myocardial infarction, arteriosclerosis, inflammation, apoplexy, angina pectoris, restenosis after angioplasty, claudicatio intermittens, migraine, tumours, tumour diseases and/or tumour metastases, in combination with at least one further medicament active ingredient.

18. Intermediate compounds of the formula II-1



II-1

in which

X-Y-D-E	denotes	CH=CH-CH=CH, N=CH-CH=CH, CH=N-CH=CH, CH=CH-N=CH, CH=CH-CH=N, N=CH-N=CH, CH=N-CH=N, NH-CO-CH=CH, CH=CH-CO-NH, CO-NH-CH=CH, CH=CH-NH-CO, in which the H atoms of the -CH- groups may be substituted by Hal, A, OH, OA, A-COO-, Ph-$(CH_2)_n$-COO-, cycloalkyl-$(CH_2)_n$-COO-, A-CONH-, A-CONA-, Ph-CONA-, N_3, NH_2, NO_2, CN, COOH, COOA, $CONH_2$, CONHA, $CON(A)_2$, O-allyl, O-propargyl and/or O-benzyl,
Ph	denotes	phenyl which is unsubstituted or mono-, di- or trisubstituted by A, OA, OH or Hal,
R^1	denotes	Hal, -C≡C-H, -C≡C-A, OH or OA,
A	denotes	unbranched, branched or cyclic alkyl having 1-10 C atoms, in which, in addition, 1-7 H atoms may be replaced by F and/or chlorine,
Hal	denotes	F, Cl, Br or I,
n	denotes	0, 1, 2 or 3,

and salts thereof.

19. Intermediate compounds according to Claim 18 in which

X-Y-D-E	denotes CH=CH-CH=CH, N=CH-CH=CH, CH=N-CH=CH, CH=CH-N=CH, CH=CH-CH=N, N=CH-N=CH, CH=N-CH=N, in which the H atoms of the -CH- groups may be substituted by Hal, OH and/or OA,
R^1	denotes Hal,
A	denotes unbranched, branched or cyclic alkyl having 1-10 C atoms, in which, in addition, 1-7 H atoms may be replaced by F and/or chlorine,
Hal	denotes F, Cl, Br or I,

and salts thereof.